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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,010	11/22/2005	Chris Robert Lively	036481-0164	8892

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FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,010	LIVELY ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32 and 37-71* is/are pending in the application.

4a) Of the above claim(s) *8-11 and 47-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 12-32, 37-46, and 67-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response and amendment of 3/5/08 have been entered.

Claims 33-36 are cancelled.

Claim 37 is amended.

Claims 1-32 and 37-71 are presently pending.

Election/Restrictions

Commensurate with the election in the reply of 6/11/07, Claims 8-11 and 47-66 remain withdrawn as being drawn to non-elected inventions.

This application contains claims 8-11 and 47-66 drawn to an invention nonelected with traverse in the reply filed on 6/11/07. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Commensurate with the election in the reply of 6/11/07, Claims 1-7, 12-32, 37-46, and 67-71 are presently considered.

Claim Status, Cancelled Claims

In light of the cancellation of Claims 33-36, all rejections and/or objections to such claims are rendered moot, and thus, are withdrawn.

Claim Objections

In light of the amendment to Claim 37, and cancellation of Claims 33-36, the objection to Claim 37 for not being further limiting is rendered moot, and thus, is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7, 12-13, 17-20, 22-30, 32, 37, 38, 42-45, and 67 remain rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,204,253 to Sanford, et al., and Balhorn, et al. (2000) Molecular Reproduction and Development, 56: 230-34, as evidenced by Oard (1993) Plant Cell, Tissue and Organ Culture, 33(3): 247-50, for reasons of record.

The reasoning is repeated for clarity of record:

With regard to Claims 1-3, 7, 13, 17-18, 25, 27, 28, 32, 38, 42-43 Sanford teaches M-10 series tungsten microprojectile particles (which range from 0.3 to 2.1 micrometers in diameter (e.g., Oard (1993) Plant Cell, Tissue and Organ Culture, 33(3): 247-50, p. 249, col. 1, paragraph 3), coated with DNA condensed in the presence of spermidine, and also in the presence of EDTA (e.g., col. 15, paragraph 2) and also in the presence of calcium chloride (e.g., Id.), and the methods of making claimed (e.g., Id.).

With regard to Claims 4-5, 28-29, Sanford teaches that a transgene for, *inter alia*, kanamycin resistance, is transformed into the cells, and further expressed (EXAMPLE 2). Kanamycin is a fungal protein, and hence, a Fungal antigen.

With regard to Claims 19-20, 44-45, the particles are subsequently contacted with ethanol (e.g., col. 15, paragraph 3).

With regard to Claims 22-24, Sanford teaches a needless syringe device, as it has no needle, but injects the particles into cells (e.g., Figure 1), and which contains a receptacle containing the particles for delivery (e.g., FIGURES 5a-5b).

With regard to Claim 26, Sanford teaches the addition of the spermidine to the mixture containing the microparticles and DNA (e.g., col. 15, paragraph 2).

However, with regard to all rejected claims, Sanford fails to teach the use of arginine of the formula $[Arg]_{2\text{-}10}$ or a physiologically acceptable salt thereof .

However, the purpose of spermidine in condensing the DNA is to provide compact particles, resistant to degradation, as taught in the Art by Balhorn, et al. (2000) Molecular Reproduction and Development, 56: 230-34, e.g., p. 230, paragraph bridging columns. Further, Balhorn teaches that transformations of somatic cells and sperm are improved by the faster release of the DNA from condensation by the use of small polymers of polyArginine, and specifically, for the highest change in off-rate, those between 6-12 arginines having the greatest release kinetics (e.g., p. 233, paragraph bridging columns). Still further, Balhorn teaches that by simply changing the amount of arginines in the polyArginine in such delivery methods, the

length of time required to dissociate from the polyArginine could be tailored for each individual delivery system (e.g., p. 233, column 2, paragraph 2).

Further, with regard to the presence of EDTA on the surface of the particle (e.g., Claim 67), absent reason to believe otherwise, these particles do have EDTA on their surface.

Hence, at the time of invention, it would have been obvious to modify the microprojectile particles of Sanford with the use of the polyarginines of Balhorn, to arrive at the claimed invention. The Artisan would have been motivated to do so to arrive at the desired release kinetics for any specific system. Moreover, the Artisan would have had a reasonable expectation of success, as Balhorn had already demonstrated the release kinetics to be improved.

Response to Argument – Sanford/Balhorn evidenced by Oard

Applicant's argument of 3/5/08 has been fully considered but is not found persuasive.

Applicant argues that neither Sanford or Oard taught or suggested the use of polyArginine polymers, and neither taught or suggested altering ingredients to increase attachment/stability of particles (p. 11, last 3 paragraphs).

Such is not persuasive. First, as taught by Balhorn, there was motivation to make the compositions and methods, and second, Applicant's claims are simply drawn to the composition and method of making, and the Art cited makes obvious the same compositions and method steps. With regard to attachment/stability, such language is not within Applicant's claims, and hence, there is no need to consider such in making the rejections. Moreover, the same composition, arrived at with proper motivation, even though such motivation may be distinct from Applicant's motivation, is still properly rejected.

Applicant argues that Balhorn provides an analysis of DNA condensation by Arg-rich peptides, that the Arg content affects release upon cellular entry, and that the authors suggest that the faster release could be achieved by using small polymers of polyArg, and specifically, domains less than 12 Arg residues long, but does not suggest its use in attaching DNA to inert particles, let alone the benefits of such (p. 12, paragraphs 1-2).

Such is not persuasive. First it should be noted that one of the best release kinetics were found with a peptide consisting of 6 Arg residues (e.g., TABLE 1), which far surpasses that the other proteins used, such as salmine and spermine (e.g., Id.). Still further, motivation is found for the same compositions, as Balhorn specifically demonstrates much faster release kinetics for Arg_6, and hence it is obvious.

Applicant broadly avers that the improvement in attachment is not found by the combination of references cited (p. 13, paragraph 3).

Such is not persuasive. First, Applicant has not claimed a method of improved attachment, but simply a composition and method of making, and hence, the improved attachment is not needed to be considered. Second, the motivation arrives at the same steps and composition.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7, 12-15, 17-30, 32, 37-40, 42-46, and 67 remain rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,204,253 to Sanford, et al., and Balhorn, et al. (2000) Molecular Reproduction and Development, 56: 230-34, as evidenced by Oard (1993) Plant Cell, Tissue and Organ Culture, 33(3): 247-50, as applied to claims 1-5, 7, 12-13, 17-20, 22-30, 32-38, 42-45, and 67, above, and further in view of Oard (1993) Plant Cell, Tissue, and Organ Culture, 33(3): 247-50 and Cherng, et al. (1999) Pharmaceutical Research, 16(9): 1417-23, for reasons of record.

With regard to Claims 1-5, 7, 12-13, 17-20, 22-30, 32-38, 42-45, and 67, as is shown above, Sanford and Balhorn, as further evidenced by Oard, make obvious the various aspects of the claims.

However, Sanford and Balhorn, as further evidenced by Oard, do not make obvious the use of gold particles, further condensed in the presence of sucrose.

On the other hand, Oard teaches the use of gold particles can reduce particle clumping (e.g., p. 249, paragraph bridging columns). Further, Cherng teaches that condensation of nucleic acids with cationic polymers is further stabilized for storage by the presence of sucrose during the condensation (e.g., ABSTRACT).

Hence, at the time of invention, it would have been obvious to modify the techniques of Sanford and Balhorn, as further evidenced by Oard, to use the gold particles of Oard to reduce clumping, and further to condense the DNA in the presence of sucrose as taught by Cherng, to increase the stability of the condensed DNA over time. Moreover, the Artisan would have had a reasonable expectation of success, as Oard teaches that gold particles will reduce clumping and Cherng taught that the sucrose present in the condensed solution would provide more stability.

Response to Argument – Sanford,Balhorn,Oard, Cherng

Applicant's argument of 3/5/08 has been fully considered but is not found persuasive.

Applicant argues that Oard states that the use of the gold flakes and poly-L-Lysine did not reduce clumping entirely (p. 14, paragraph 2), implying that the Artisan would not use it if it was not 100% effective.

Such is not persuasive. The Artisan would be interested in reducing clumping as much possible, and if it is not 100% perfect, the Artisan would reduce it as much as possible.

Applicant argues that Cherng is specific to their lyohpylizations and polyplexes, and does not teach or suggest the use of such in the metal carrier type compositions and methods presently claimed (p. 14, paragraphs 3-4).

Such is not persuasive. It is clear that sucrose stabilizes such nucleic acid/protein complexes and that aging for 10 months in aqueous solutions comprising sucrose stabilized them (ABSTRACT). The other findings are simply irrelevant to the rejection. Moreover, motivation need not be specifically suggested in the references and the Art is taken from the viewpoint of the Artisan, who would understand such to mean that similar compositions would stabilized by sucrose. Lastly, there is no reason to believe it would not work when a metal particle is also included.

Applicant broadly avers that Cherng would require the obvious invention to be the carriers with the polyplex DNA of Cherng (pp. 14-15, paragraph bridging).

Such is not persuasive. Motivation need not be specific, nor need it be specifically limiting to the specific thrust of any of the individual teachings.

Applicant boadly avers that the various art would not arrive at the rejected invention (p. 15, paragraph 2).

Such is not persuasive. The Examiner arrived at the same limitations through a proper rejection, so the Artisan would arrive at the rejected invention. Broad argument does not supplant the need for specific reasoning and/or evidence to rebut the Examiner's argument.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

While the previous rejections did not specifically disclose raffinose, and hence, are withdrawn, Claims 1-7, 12-32, 37-46, and 67-71 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over .S. Patent No. 5,204,253 to Sanford, et al., and Balhorn, et al. (2000) Molecular Reproduction and Development, 56: 230-34, as evidenced by Oard (1993) Plant Cell, Tissue and Organ Culture, 33(3): 247-50, and further in view of Oard (1993) Plant Cell, Tissue, and Organ Culture, 33(3): 247-50 and Cherng, et al. (1999) Pharmaceutical Research, 16(9): 1417-23, as applied to claims 1-5, 7, 12-15, 17-30, 32-40, 42-46, and 67 above, and further in view of U.S. Patent Publication No. 2004/0142475 to Barman, et al, as further evidenced by U.S. Patent No. 6,194,136 to Livesey, et al.

As shown above, Claims 1-5, 7, 12-15, 17-30, 32-40, 42-46, and 67 are obvious over the Art cited, except the cited Art does not specifically teach the use of transgenes encoding

therapeutic proteins, or the use of a combination of raffinose and sucrose to stabilize the DNA. Nor does the cited art teach or make obvious the transgenes encoding HPV, HIV, HSV2, HSV1 or Hepatitis B antigens.

On the other hand, Barman teaches that stabilizers such as saccharides may be used in combination to stabilize the nucleic acid protein complexes (e.g., paragraph 0054). Further, Barman teaches that HPV, HIV, HBV, and HSV (which includes HSV1 and HSV 2), antigens can be the transgenes for expression of antigens (paragraph 0036). Still further Livesey also demonstrates the general understanding in the Art that various stabilizers which are sugars include raffinose (DESCRIPTION OF THE PREFERRED EMBODIMENTS, paragraph 29).

Hence, at the time of invention, it would have been obvious to modify the cited Art with Barman to use both raffinose and sucrose in stabilizing the particles and/or to use the various cited virus proteins. The Artisan would have been motivated to do so as the art already recognized that the sugars could be used in combination and/or the various proteins could be expressed for making antigens. Moreover, the Artisan would have had a reasonable expectation of success, as the Art already recognized the efficacious effect of saccharides.

Response to Argument – Sanford,Balhorn,Oard, Cherng, Barman

Applicant's argument of 3/5/08 has been fully considered but is not found persuasive.

Applicant argues that Barman's agents were encapsulated within the microparticles to facilitate delivery (p. 15, penultimate paragraph). Further, Barman did not discuss raffinose (pp. 15-16, paragraph bridging).

Such is not persuasive. While Barman did not specifically disclose raffinose, sugars have been long known as stabilizers of nucleic acids and proteins, and now Livesey is utilized to make

the rejection. However, as Barman did not specifically disclose raffinose, the present action is non-final. Still further, the purpose of supercoiled DNA as Applicant interprets Barman, is one of protection, which is stabilization, and hence, the motivation still exists to utilize the substances claimed.

Applicant argues that Barman does not teach how the sugars will work when the DNA is applied to an inert particle (p. 16, paragraph 2).

Such is not persuasive. If the particle is inert, it will not alter the stabilization. There simply exists no reason to believe it would not work, and further, broad argument otherwise does not supplant the need to demonstrate a flaw in logic or evidence to the contrary.

Applicant argues that Barman provides no specific motivation to arrive at the instantly claimed invention (p. 16, paragraph 3).

Such is not persuasive. Motivation need not be specific. Motivation is amply supplied by the Examiner. Moreover, the logic and reasoning is sound.

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Acting Examiner of Art Unit 1633